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PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number: 00786-421002
I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to Mail Stop AF, Commissioner for Patents, Box 1450, Alexandria, VA 22313-1450. July 18, 2006 Date of Deposit Carri A. Amonte Signature Carri A. Amonte Typed or Printed Name of Person Signing Certificate	Application Number 10/019,837	Filed September 10, 2002
	First Named Inventor Nikolaos Soukos et al.	
	Art Unit 3734	Examiner E. Cameron

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a Notice of Appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)

☒ attorney or agent of record 41,942
(Reg. No.)

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34

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July 18, 2006
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below'.

☐ Total of **no.** forms are submitted.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Nikolaos Soukos et al.
Serial No. : 10/019,837
Filed : September 10, 2002
Title : PERMEABILIZING BIOFILMS

Art Unit : 3734
Examiner : E. Cameron

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRE-APPEAL CONFERENCE BRIEF

Applicant submits that there has been a clear factual error in the Examiner's rejections under 35 U.S.C. §103 over *Flotte*. In particular, Applicant submits that a careful reading of *Flotte* will reveal fundamental flaws in the Examiner's understanding of *Flotte* and the applicability of its teachings. Additionally, Applicant submits that the rejections under 35 U.S.C. §112 made by the Examiner evince an incomplete or flawed understanding of the teachings of the specification.

Section 103 rejection – Claim 1

The Examiner states that "Flotte teaches laser-induced stress transients ... that aid molecules crossing **cell membranes** by increasing cell permeability."[1] Thus, the Examiner apparently concedes *Flotte*'s failure to teach "delivering a compound into **a matrix of a biofilm**" as recited in independent claim 1.[2]

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[1] *Final Office Action of January 18, 2006*, page 6 (emphasis added).
[2] Similarly, the Examiner apparently concedes that *Flotte* does not teach "permeabilizing a biofilm" as recited in independent claim 25, and "delivering a therapeutic agent into a matrix of the biofilm" as recited in independent claim 26 (emphasis added). In the interest of brevity, we do not elaborate on our arguments regarding claims 25 and 26, but note that the arguments made here in connection with claim 1 apply to claims 25 and 26, *mutatis mutandis*.

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

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July 18, 2006
Date of Deposit

Carni A. Amonte
Signature

Carni A. Amonte
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In rejecting these claims, the Examiner reasons that "cells would be inclusive of the bacterial cells in a biofilm."[3] Apparently the Examiner makes no distinction between delivering a compound into a matrix of a biofilm, and delivering a compound into a cell membrane that happens to be embedded within, but distinct from, the matrix of the biofilm.

However, as the Applicant has previously observed,[4] *Flotte* teaches that stress waves cause aqueous pore formation in cell walls.[5] According to *Flotte*, it is these pores that account for the increased permeability in cells.[6]

In contrast, the matrix of a biofilm lacks a cell wall. Therefore, one of ordinary skill would hardly expect, based on *Flotte*, that the mechanism by which a cell wall is permeabilized is applicable to the a matrix of a biofilm. Indeed, the teachings of *Flotte* and the structural disparity between a matrix of a biofilm and a cell wall suggest that, in fact, the matrix of the biofilm would be immune to the permeabilizing procedure prescribed by *Flotte*.

In response to the Applicant's observation, the Examiner maintained that "[b]acteria have cell walls and therefore it is expected that biofilms have cell walls as part of their makeup."[7] The Examiner's logic appears to be that, since *Flotte* teaches delivery through cell walls, and since biofilms contain bacteria, which in turn have cell walls, then *Flotte* teaches delivery into a biofilm.

But the claim recites delivery specifically into a matrix of a biofilm. The matrix and the cells are different. As the specification makes clear,

> [b]iofilms are typically matrix-**enclosed** microbial aggregates associated with each other and a solid surface. Bacteria within biofilms have an increased resistance to antimicrobial agents relative to that of planktonic [i.e., non-matrix-enclosed] cells of the same species. The relative impermeability of biofilms to compounds such as antimicrobial agents may be one reason why microbial infections associated with biofilms are difficult to treat.[8]

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[3] *Final Office Action of January 18, 2006*, page 7.
[4] See *Amendment in Reply to Action of September 12, 2005*, page 10.
[5] *Flotte*, p. 162.
[6] *Id.*
[7] *Final Office Action of January 18, 2006*, page 7.
[8] *Specification*, p. 1, lines 12-20 (emphasis added).

Thus, not only is the matrix of a biofilm structurally dissimilar from the cells it encloses, but it stands as an obstruction to those cells. In a biofilm, even if one to permeabalize the microbes, as taught by *Flotte*, the now-permeabalized microbes are still enclosed by a matrix whose permeability is not discussed in *Flotte*. Moreover, the teachings of *Flotte* suggest that the matrix's permeability remains unchanged, because it lacks the structure described in *Flotte* to account for the microbes' increased permeability.

By way of analogy, the Examiner seems to argue that a reference describing how to unlock a door to a castle makes it perfectly obvious how to cross a deep moat that surrounds the castle in order to get to the door. In the pending claims, even if "biofilms have cell walls" within them, as the Examiner suggests, the rejected claims recite delivery into **a matrix** of a biofilm, and not a cell embedded in a matrix of that biofilm in gross. Accordingly, the Applicant submits that the Examiner's rejection under 35 U.S.C. §103 is improper.

Section 112 rejections

1. *Claim 1 - Absence of a Coupling Medium is Enabled*

The specification indicates that "[f]iber optic delivery systems are particularly maneuverable and can be used to irradiate target materials located **adjacent to biofilms** to generate stress waves in remote, otherwise inaccessible locations."[9] The case in which a target material is adjacent to a biofilm is precisely a case in which there is no coupling medium.

2. *Claim 1 - Absence of a Target Material is Enabled*

Page 7 discloses a variety of ways to generate stress waves none of which require a target material. These include using lithotripters, transducers, explosive reactions in energetic materials, and fiber optics. Any of these alternative methods can be used, e.g., to "propagate a sufficient number of stress waves into the biofilm..." as recited in claim 1.

[9] *Specification*, p. 7, lines 26-28 (emphasis added).

3. *Claim 15 - The Terms "Capsular" and "Capsular Polysaccharide" are not Vague*

Applicant submits that the terms "capsular" and "capsular polysaccharide" have well-defined meanings in the art. By way of example only, some microbes sometimes produce a layer of polysaccharides. This layer is referred to as a "capsule." Capsular polysaccharides are polysaccharides that can be found in this layer.

4. *Claims 1 and 24 - "Matrix of a Biofilm" is not New Matter*

The specification states that "[b]iofilms are matrix-enclosed microbial aggregates associated with each other and a solid surface."[10] The Applicant submits that at least this sentence adequately supports claims reciting "a matrix of a biofilm." Namely, the matrix is that which encloses the microbial aggregates in a biofilm. To argue otherwise would be as disingenuous as suggesting that the statement "a pie is a crust-enclosed filling" only discloses a filling, and not a crust.

5. *Claim 24 - Entering the Matrix of a Biofilm is not New Matter*

"The examiner cannot find in the specification the concept that the antimicrobial agent enters a 'matrix' of a biofilm rather than the biofilm itself."[11] Since a biofilm is a matrix-**enclosed** microbial aggregate, when something enters a biofilm, it necessarily enters the biofilm's matrix.

6. *Claim 22 - "Associated with" is not Unclear*

The Applicant submits that the meaning of "associated" can be found in the discussion beginning on page 5, line 8 and ending on page 6, line 11, in which biofilms are described as being found "in association with" various surfaces and conditions. The Examiner appears to interpret "associated" in claim 22 as calling for a structural relationship ("Does it mean that the biofilm is attached to the surface, near the surface, a part of the surface?")[12] On the contrary, the phrase "associated" should be understood in the context of pages 5-6 of the specification. For

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[10] *Specification*, p. 5, lines 5-7.
[11] *Final Office Action of January 18, 2006*, p. 4.
[12] *Final Office Action of January 18, 2006*, p. 5

example, a biofilm is associated with a surface if the biofilm is a byproduct of organisms living on the surface. This is, of course, not the only condition in which a biofilm may be "associated" with a surface.

7. *Claim 19 - "Suitable for Mixing with" is not Unclear*

The Examiner does not appear confused as to what is being claimed, but instead appears confused as to the **consequences** of performing the steps that are clearly recited in claim 19.[13] The Applicant submits that the claim language is clear and unambiguous. There is no requirement that the Applicant indicate, in addition to the claimed steps, any consequence that results from performing the claimed steps.

Summary

Applicant encloses a check for the notice of appeal and a petition for extension of time. No additional fees are believed to be due. However, to the extent fees are due, or if a refund is forthcoming, please adjust our deposit account 06-1050, referencing attorney docket 00786-421002.

Respectfully submitted,

Date: July 18, 2006

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[13] "[I]t is not clear if the mixing actually occurs or not." *Final Office Action of January 18, 2006*, p. 5